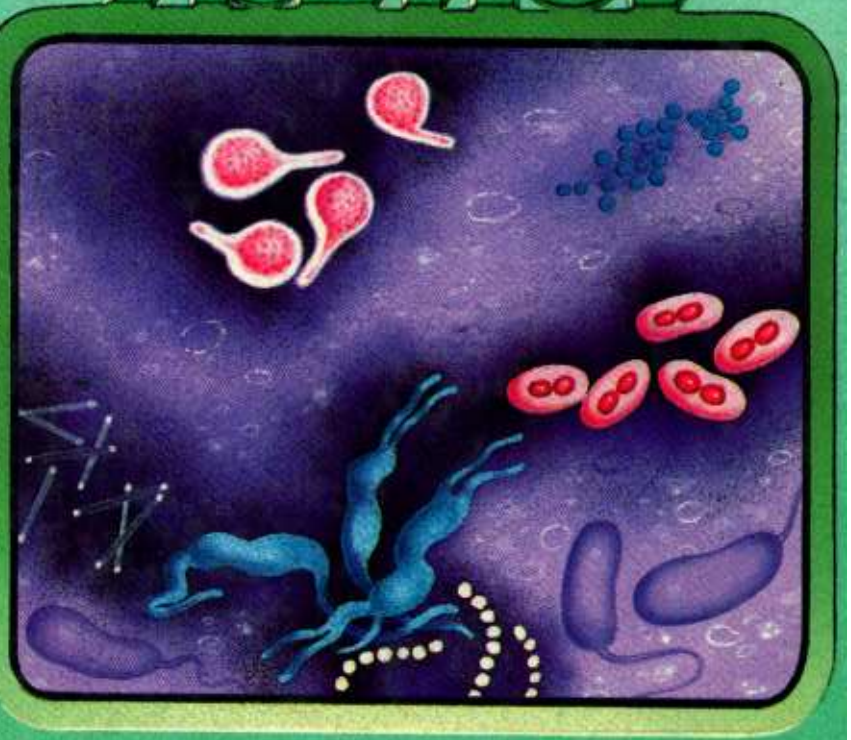
ISAAC ASIMOV



How we found out about

Germs

HOW WE FOUND OUT ABOUT

GERMS

Isaac Asimov

Contents

1. HOW GERMS WERE DISCOVERED 7
2. WHERE GERMS COME FROM 16
3. DISEASE 24
4. GERMS AND DISEASE 33
5. THE SMALLEST GERMS 45

INDEX 53

1. How germs were discovered

In the ancient Latin language any tiny bit of life from which a much larger living thing (or "organism") can develop was called a "germen". In English, the word was shortened to "germ".

But how small can a germ—any tiny bit of life—be?

At first, the smallest bits of life people knew about were certain tiny seeds out of which plants grew. They were barely large enough to see. Could there be living bits of life too small to see? How could anyone know?

Of course, there were ways to make things seem larger. In ancient times, some people had noticed that when you looked at objects through pieces of curved glass, they appeared larger.

It was not until about 1650, though, that scientists carefully studied small things after making them appear larger by looking at them through bits of curved glass. Such bits of curved glass were called "lenses" from a Latin word meaning "lentil" because they were shaped like lentil seeds.

When small living things were looked at through lenses, they appeared much larger. Many details of their bodies could be seen clearly that could not be seen without lenses.

More than one lens was usually used, and they were placed at opposite ends of a metal tube so they would stay in the proper position for seeing. Such a tube was called a "microscope" from Greek words meaning "to see small things". Lots of tiny, living, creeping things were looked at—especially fleas. For this reason the earliest microscopes were called flea glasses.

These first microscopes were quite poor. The glass used for the lenses was not very good. It had bubbles in it and the surface of the lens was not very smooth. Anything that was enlarged by the use of such lenses looked a little fuzzy. If stronger lenses were used to enlarge it still more, everything got so fuzzy that nothing could be seen at all.

In the Netherlands, Anton van Leeuwenhoek was doing his best to improve lenses. He was not a trained scientist since he had had very little education. He owned a hardware store and served as custodian at the city hall of his home town.

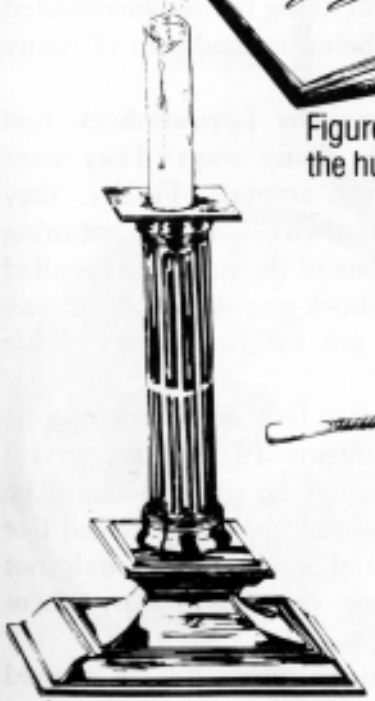
But really what he cared about was making lenses. He carefully picked out small bits of glass that had no bubbles in them at all. Then he polished them until the surface was very smooth and evenly curved. The lenses were small, but when he looked through them he found that the objects he looked at appeared to be enlarged up to 200 times and still seemed sharp.

Altogether he made 419 microscopes and lenses. Making one was very slow work because of the careful way he went about it. Still, he lived to be 90 years old and he worked his whole life!

Anton van Leeuwenhoek experimented with a microscope

Figures of bacteria from the human mouth

Single lens microscope



Leeuwenhoek used his excellent little lenses and microscopes to look at insects, skin, blood, hair, and anything else he could find. In 1677, he even sucked up a little drop of water from a pond and looked at it through one of his small lenses. He saw tiny little things in the water.

They were very tiny, less than a twentieth of a centimetre in size, but they moved about and ate things. They were *living*, even though they were too small to see without a microscope. No person before Leeuwenhoek had ever suspected that such tiny living things existed.

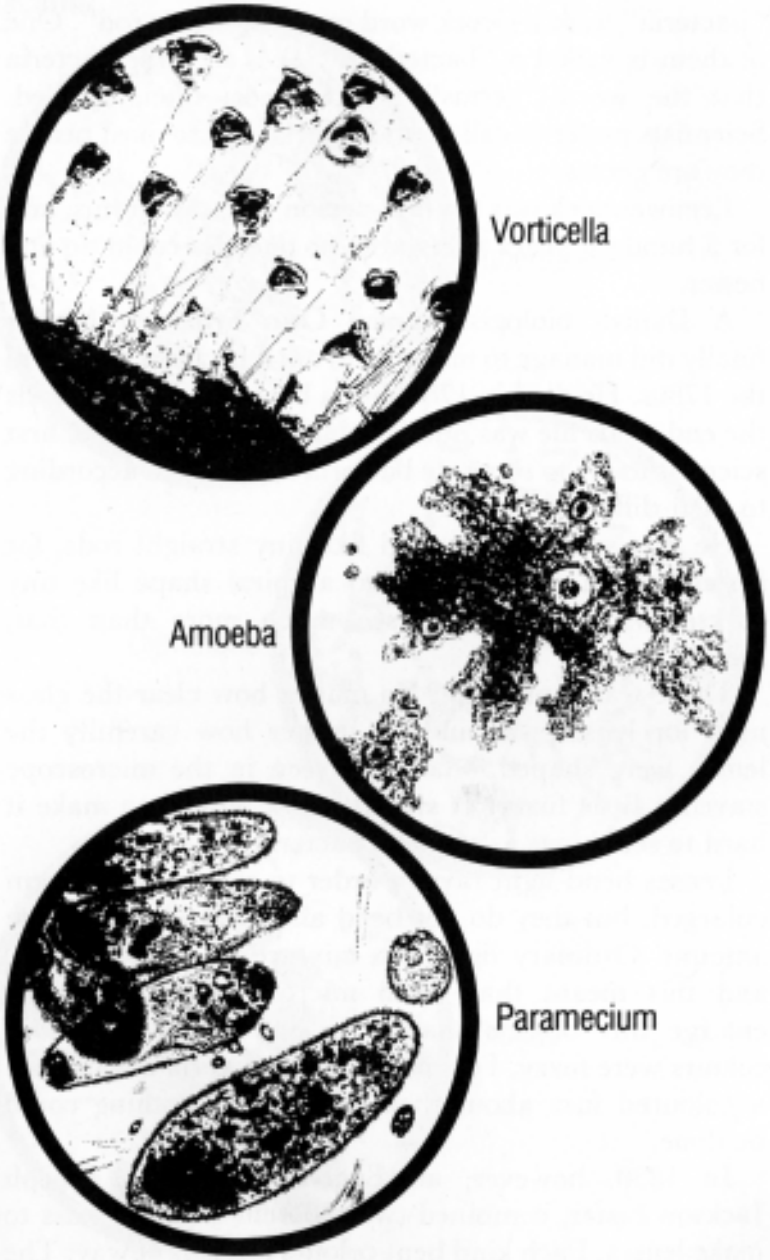
Any living creature too small to be seen without a microscope is now called a "micro-organism". Leeuwenhoek was the first person to see micro-organisms. A micro-organism is usually made up of a single cell which is a tiny bit of living matter surrounded by a membrane. A human being is made up of many millions of millions of cells.

The particular micro-organisms Leeuwenhoek first saw behaved like animals in many ways. They were therefore considered very tiny animals. Finally, they were named "protozoa" from Greek words meaning "earliest animals". A single one of the protozoa is called a "protozoon". But Leeuwenhoek was sure that the tiny protozoa he saw first were not the tiniest bits of life there were.

Every time he made a better lens or microscope he could see smaller micro-organisms. In 1683, he used a lens that showed him tiny things he thought might be alive. They were so tiny, however, that they looked like small dots and rods but nothing more. He just could not make a lens that was strong enough to show them clearly, and he had to give up.

Eventually, those tiny things he saw were named

Different kinds of protozoa



"bacteria" from a Greek word meaning "little rod". One of them is called a "bacterium". It is to these bacteria that the word "germs" is now most often applied. Scientists prefer to call them bacteria, but to most people they are germs.

Leeuwenhoek was the first person who saw germs, and for a hundred years afterwards no one else could do any better.

A Danish biologist named Otto Friedrich Muller finally did manage to make them out a bit more clearly in the 1780s. He died in 1784, but a book he wrote towards the end of his life was published in 1786. He was the first scientist to try to separate bacteria into groups according to their different shapes.

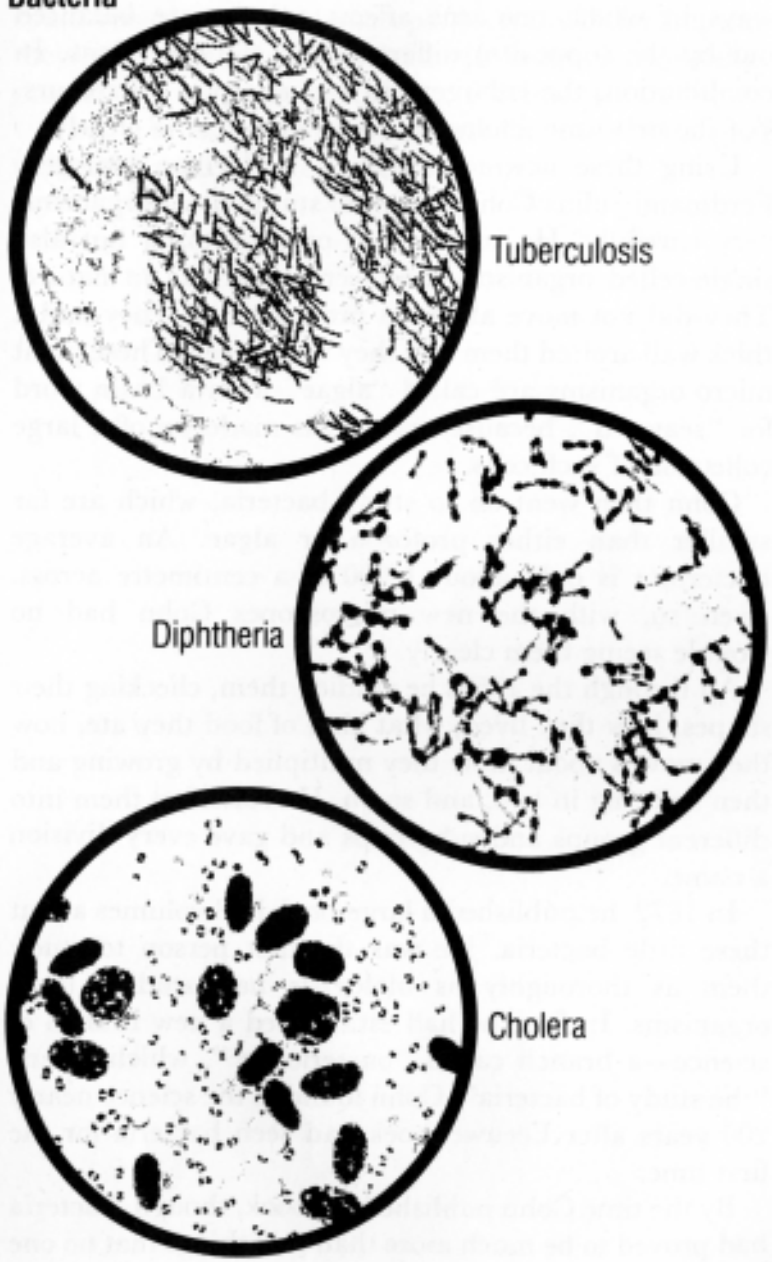
He saw some that looked like tiny straight rods, for instance, and others that had a spiral shape like tiny corkscrews. He couldn't see much more than that, though.

There was a problem. No matter how clear the glass used for lenses was and no matter how carefully the lenses were shaped, what was seen in the microscope stayed a little fuzzy. It stayed fuzzy enough to make it hard to see things as small as bacteria.

Lenses bend light rays in order to make objects seem enlarged, but they do not bend all colours by the same amount. Ordinary light is a mixture of many colours, and this meant that when microscopes managed to enlarge tiny objects sharply in one colour the other colours were fuzzy. For that reason, bacteria always had a coloured fuzz about them. It seemed nothing could be done.

In 1830, however, an English lensmaker, Joseph Jackson Lister, combined two different kinds of glass to make lenses. Each kind bent colours a different way. The

Bacteria



ways in which one lens affects colours are balanced out by the (opposite) differences in the other lens. In combination, the enlargement was sharp in all colours. For the first time, biologists could see bacteria clearly.

Using these new microscopes, a German biologist, Ferdinand Julius Cohn, began to study micro-organisms very carefully. He studied not only protozoa but also single-celled organisms that were plant-like in nature. They did not move about as protozoa did. They had a thick wall around them and they were green. These plant micro-organisms are called "algae" from a Latin word for "seaweed", because seaweed is made up of a large collection of such cells.

Cohn then went on to study bacteria, which are far smaller than either protozoa or algae. An average bacterium is only about 1/200 of a centimetre across. Even so, with the new microscopes Cohn had no trouble seeing them clearly.

All through the 1860s he studied them, checking their shapes, how they lived, what kind of food they ate, how they moved about, how they multiplied by growing and then splitting in two, and so on. He classified them into different groups and subgroups and gave every division a name.

In 1872, he published a large book in 3 volumes about these little bacteria. He was the first person to study them as thoroughly as biologists had studied large organisms. In fact, he had established a new branch of science—a branch called "bacteriology", which means "the study of bacteria". Cohn founded the science nearly 200 years after Leeuwenhoek had seen bacteria for the first time.

By the time Cohn published his book, though, bacteria had proved to be much more than tiny things that no one

could see without a microscope. In spite of the fact that they were so tiny and invisible to ordinary eyes, they proved to be of great importance to humans.

They became so important because biologists wondered where bacteria came from.

2. Where germs come from

People had been wondering where many kinds of organisms came from. In the case of large plants and animals there was no problem. Everyone knew that animals gave birth to live young or laid eggs. Everyone knew that plants grew from seeds. They knew that each plant and animal came from other plants and animals like itself. Oak trees came from oak trees, dogs came from dogs, human beings came from human beings.

Bugs and worms, though, were something else. They seemed to come from nowhere. Some people felt that these simple little forms of life arose from dead matter. Somehow, they felt dead matter could become alive without help from the outside. This was called the theory of "spontaneous generation".

A good example of spontaneous generation was what happened to ordinary meat when it decayed. From nowhere, it seemed, little worms called maggots appeared on it. Those maggots, people said, arose from the dead meat by spontaneous generation.

In 1668, however, an Italian biologist, Francesco Redi, thought he would try an experiment. After all, there were always flies around the decaying meat. Perhaps they had something to do with the maggots.

What Redi did was to put pieces of meat at the bottom of little pots to decay. The pots were open on top, but on half of them Redi stretched pieces of gauze. Flies could get into the pots without the gauze and land on the meat. They could not get to the meat in the pots protected by the gauze.

All the pieces of meat decayed in the same way, but maggots developed *only* in the pieces on which flies landed. The meat that was protected by gauze never developed maggots, no matter how it decayed.

Redi decided that flies laid eggs on the decaying meat and the maggots came out of those tiny eggs. They fed on the meat and eventually changed into flies in the way that caterpillars change into butterflies.

By using microscopes, it was finally possible to see the eggs that flies laid in the meat. Could it be that *all* organisms, even insects and worms, came out of eggs laid by other insects and worms? Could it be that living things only came from other living things and never from dead matter? Was it possible that the theory of spontaneous generation was wrong?

Biologists might have abandoned the notion of spontaneous generation, but not long after Redi's experiment Leeuwenhoek discovered micro-organisms. These were living things far simpler than even the simplest insect. How about them? Perhaps micro-organisms were so simple that they could form out of dead matter even though insects did not. Biologists discussed this, for a long time.

Finally, in 1748, an English biologist, John Turberville

Needham, tried an experiment.

He began with some mutton soup that had numerous micro-organisms in it. He boiled the soup for a few minutes in order to kill these micro-organisms. Then he put the boiled soup in a container which he sealed tightly.

He knew that micro-organisms could not enter the flask from outside as long as the container was sealed. Any micro-organisms that were to be found in the soup after he opened the seal would have to have arisen from the soup itself.

Needham let the sealed container stand a few days. Then he opened it and found that the soup was swarming with living micro-organisms. Needham was certain that this proved that the theory of spontaneous generation was true, at least for microscopic organisms.

Fly

Eggs

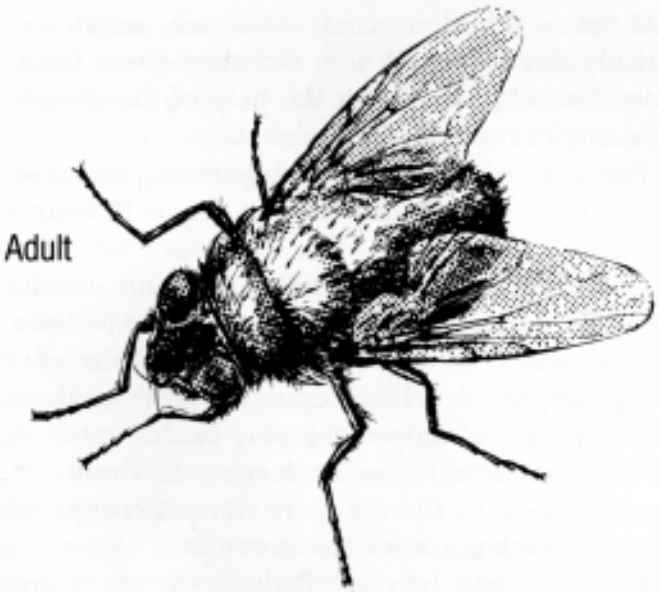
Maggot

But did the experiment settle matters really? An Italian biologist, Lazzaro Spallanzani, was not at all sure. He wondered if Needham had boiled the soup long enough. Some of the micro-organisms might be pretty tough and a few might survive. Needham might not have seen the few micro-organisms that were still alive, and they might have multiplied while the soup was standing in the sealed container.

In 1768, Spallanzani began to test how long it took to kill micro-organisms by boiling. He found that some were indeed hard to kill. He found that it was not safe to suppose that all the micro-organisms were dead unless the soup was boiled for at least half an hour.

He then repeated Needham's experiment, but he boiled the soup for half an hour, or even more, before sealing it. He found that when this was done the soup

Adult



could stand for long periods of time and never develop any micro-organisms. The soup remained "sterile"—that is, without any life in it at all.

In Spallanzani's experiment, it seemed that there was no spontaneous generation after all. Even tiny micro-organisms developed only from living matter, from other micro-organisms like themselves.

But again not everybody was convinced. Some biologists argued that the boiling did not happen in nature. Perhaps spontaneous generation worked through some chemical in the air. Perhaps boiling destroyed that chemical, and that was why spontaneous generation did not take place after boiling. It might be that Needham's boiling had only destroyed some of the chemical, so that spontaneous generation could still take place. Spallanzani's longer boiling, however, destroyed all of the chemical.

After all, these biologists said, if you took boiled soup and let it stand in cool, fresh air, micro-organisms quickly developed. Where did they come from, if not from the soup itself with the help of the chemical that was only in the cool, fresh air?

For a hundred years, biologists argued about this. Then, in 1858, a French chemist, Louis Pasteur, tackled the problem.

In the first place, he tried to find out whether cool, fresh air might not have bacteria in it. He boiled a cotton plug in water until both the cotton and the water were completely sterile. He then pumped fresh air through the cotton plug and dipped the plug in the water. At once, micro-organisms began to develop in the water. That made it seem as though there were micro-organisms in the air, which got stuck to the cotton.

Could Pasteur be sure? Perhaps the micro-organisms

arose by spontaneous generation out of the sterile cotton or the sterile water. To test this, Pasteur filtered a quantity of air through a sterile cotton plug. Then he drew this filtered air through a second sterile cotton plug and placed it in the water.

This time, no micro-organisms were found. They had all been removed from the air by the first plug and none developed in the sterile second plug or in the sterile water.

In this way, Pasteur showed that there were micro-organisms floating all about us in the air, attached to dust particles. If boiled soup was exposed to the air, it was also exposed to the floating micro-organisms on the dust. That was why micro-organisms developed in the soup.

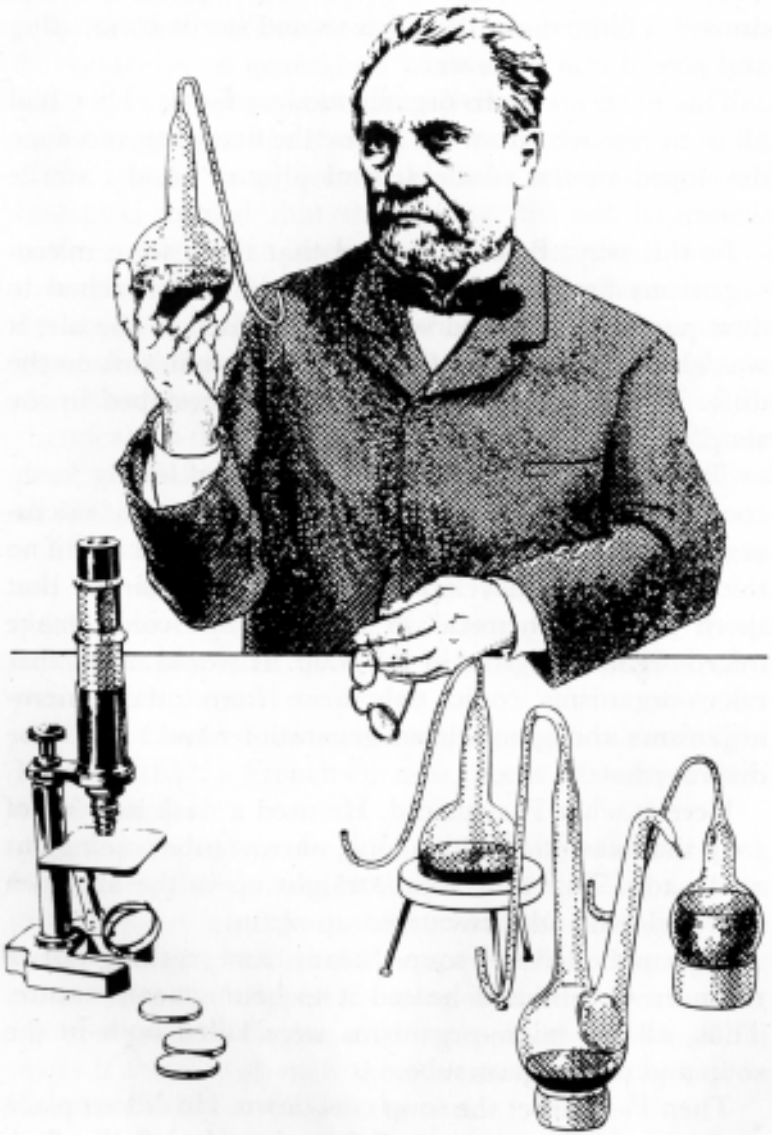
Then Pasteur tried to think of a way of letting fresh, cool air reach the soup without letting in any micro-organisms on dust particles. If he could do that and if no micro-organisms developed in the soup, it meant that there was no chemical in the air that could make micro-organisms grow in the soup. It would mean that micro-organisms could only arise from other micro-organisms and spontaneous generation would finally be disproved.

Here is what Pasteur did. He used a flask half-full of soup that was fitted with a long, narrow tube coming out of the top. This tube went straight up in the air, then curved down and then curved up again.

Pasteur boiled the soup. Steam came rushing out of the narrow tube and heated it to boiling temperature. Thus, all the micro-organisms were killed both in the soup and on the glass tube.

Then Pasteur let the soup cool down. He did *not* place a stopper in the opening of the tube. He left the flask

Louis Pasteur with his special flasks



open so that the soup within was not blocked off. Cool, fresh air could drift in and out of the flask and make contact with the surface of the soup. Dust, however, could *not* enter the flask. Dust settled down at the bottom of the curve of the tube. It could not move uphill in that narrow tube.

Pasteur then let the soup stand and did not do a thing to it. Even when he let such soup stand for months, however, no micro-organisms developed in the soup. The cool, fresh air and the chemicals in it might touch the soup, but as long as no dust, carrying micro-organisms, touched it there was no development of micro-organisms in it.

Pasteur then tried breaking off the tube of such a flask. Now dust could just fall into the soup, and overnight it was suddenly full of micro-organisms.

Pasteur announced these experiments and their results in 1864. Others tried the same experiment and got the same result.

That settled it. There was no spontaneous generation. A micro-organism comes only from another micro-organism.

This was a very important point to settle. It meant to Pasteur that, whenever he found a micro-organism where it wasn't supposed to be, *it had come from somewhere else*. It could not have arisen from anything other than another micro-organism.

He combined this knowledge with other work he had been doing and was able to make one of the greatest discoveries in the history of science. This discovery concerned disease.

3. Disease

Disease is a subject that concerns everyone. No one can ever be sure that he or she might not suddenly fall sick. A person can at any time begin to feel bad, develop a fever, or break out in a rash. Eventually, he or she might even die of a disease.

When one person falls sick, others might also. A disease can suddenly spread over a whole town or a whole region, and some diseases can be very deadly.

In the 1300s, for instance, a disease called the Black Death spread all over Europe, Asia and Africa and killed millions of people. It was the greatest disaster in human history. One-third of all the people in Europe died.

At this time nobody in the world knew what caused disease. Some people thought demons or evil spirits took over the body. Some people thought it was bad air of some sort or another. Some people thought it was a punishment from Heaven for evil deeds.

Whatever it was, though, no one imagined the diseases could be stopped and no one knew when another Black Death might strike.

One hopeful thing about disease was that some

London scene during the Black Death 1348

diseases only hit a person once. If someone caught measles or mumps or chickenpox and then got well again, that person would never get that particular disease again. He or she was "immune". His or her body had fought off the disease and had developed some kind of defence that would continue to work for many years.

One particularly dreadful disease that only struck once was smallpox. The trouble was that very often once was quite enough. Many people who caught smallpox died. Many others recovered, but their faces and bodies were covered with scars left over from the terrible blisters they had had. Every once in a while, though, someone had only a light case that did not scar him or her much. When that happened, the person was just as immune afterwards as if he or she had had a terrible case.

Naturally, it was much better to have a light case of smallpox than to have none at all. With a light case, you were safe for life; with none at all, you could never be sure you might not get it at any moment.

People knew that if you were near a person with smallpox you might catch it. Would it not be a good idea, then, to stay near a person with a light case? You might catch the light case and then be safe. To make sure, you might scratch your skin with a needle that had been dipped into some of the fluid in the smallpox blisters of the sick person. This was called "inoculation".

The trouble was, though, that a person might have a light case of smallpox, yet another person catching it might get a severe case. Inoculation was not safe.

In the 1770s, an English doctor, Edward Jenner, grew interested in a disease called cowpox. It was called that because it was found in cows and in other farm animals. The disease was something like a very mild smallpox. If a person caught cowpox from a cow, he or she would get

a blister or two and that was it. People would hardly even know they were sick.

The country people where Jenner lived thought it was good luck to get cowpox because then you never got smallpox. Most doctors thought this was just a superstition, but Jenner wondered. He did notice that people who worked with farm animals a good deal hardly ever got smallpox.

After 20 years of study, Jenner decided to try a very dangerous experiment. On 14 May 1796 he found a milkmaid who had just developed cowpox. He dipped a needle into the fluid inside a blister on her hand and scratched the skin of a boy who had never had either cowpox or smallpox. The boy got cowpox and developed a blister in the place where he had been scratched.

Jenner then waited for 2 months to make sure the boy was completely recovered. He was immune to cowpox, but was he also immune to *smallpox*? Taking an enormous chance, Jenner deliberately scratched the boy with a needle that had been dipped in the fluid of a real smallpox blister. The boy did *not* catch smallpox.

Jenner tried the whole thing again 2 years later when he found another girl with cowpox. He again found he could make someone immune to smallpox by giving them fluid from a cowpox blister.

The medical name for cowpox is "vaccinia" from a Latin word for "cow". Jenner's system for giving people cowpox to save them from smallpox was therefore called "vaccination". When Jenner announced his findings, vaccination was quickly adopted all over the world. Smallpox disappeared from places where vaccination was used.

Other diseases could not be defeated in the same way, though. No other disease seemed to have a mild cousin

Statue of Edward Jenner giving the first vaccination

that could be used to make a person immune.

Still, the whole business of vaccination made people think about the way you could transfer disease from one person to another. Maybe you could prevent people from getting sick if you stopped transferring the disease.

An Hungarian doctor named Ignaz Philipp Semmelweiss thought so. In the 1840s, he worked in a hospital where women came to have babies. Many of them died of a fever after the babies were born. Women who had their babies at home did not usually die in this way.

Semmelweiss wondered what made so many people die in the hospitals. In them, the mothers were treated by doctors who also worked on people who were sick or who had died. At home, the babies were delivered by women who did not deal with sick people. Could it be that the doctors were carrying disease from the sick patients to the mothers?

In 1847, Semmelweiss was placed in charge of a hospital, and he made a rule that all doctors had to wash their hands in a strong chemical solution before they came near a patient. At once, the situation improved. Hardly any mothers died in the hospital.

The doctors, however, were annoyed. They did not like to wash their hands in smelly chemicals and they did not like to be told that they were carrying a disease that killed people. Besides, they argued there was nothing on their hands so how could they be carrying a disease? They forced Semmelweiss out of his position. Then they stopped washing their hands and the mothers began to die again just as before.

But that was a problem. Could something invisible carry a disease?

Some years before he solved the problem of spontaneous generation, Louis Pasteur had begun a

line of study that was to answer the question.

France's wine industry was in deep trouble at that time. Wine was turning sour when it should not have been. The wine producers were losing millions of francs (French money) as a result.

In 1856, Pasteur was asked to investigate the problem. One of the things he did was to look at the wine under a microscope. He saw micro-organisms called "yeast" in the wine. That was not surprising. Yeast belonged in wine. It grew in fruit juice and turned the sugar of that juice into alcohol.

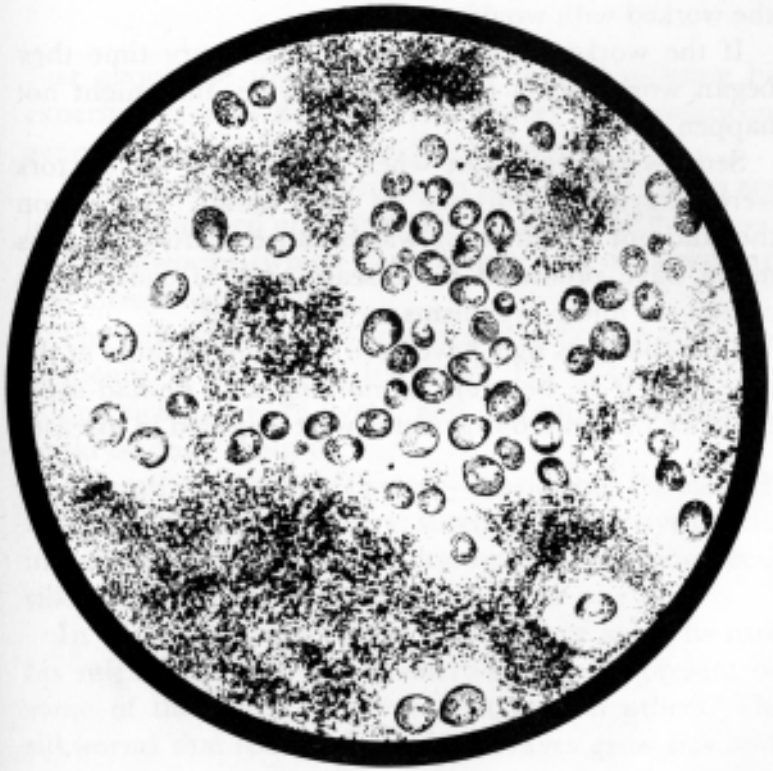
When Pasteur looked at the sour wine, though, he found that some of the yeast cells present were different in shape from the usual cells. It seemed there were two kinds of yeast. The right kind turned sugar into alcohol, and the wrong kind turned the alcohol into a kind of acid.

Yeast cells are easy to kill by gentle heating. Pasteur suggested that once the wine was formed it should be gently heated. The yeast cells would be killed. The right kind of yeast had done its work and was not needed any more. The wrong kind of yeast would be killed before it could do its acid-producing work.

The wine producers did not like to heat their wine, but they tried it. It worked. The souring of wine stopped and the wine industry was saved. Gentle heating designed to kill harmful micro-organisms has been called "pasteurisation" ever since. The milk we buy is nearly always pasteurised.

Pasteur's work on wine was one of the reasons he was sure that spontaneous generation was impossible. If spontaneous generation could happen, then killing the yeast would do no good. Both kinds of yeast would be likely to arise again and it would turn sour anyway.

Yeast cells



Pasteur could therefore move on to his great experiment on spontaneous generation quite confident that he would not grow micro-organisms out of dead matter.

The work he did with wine also showed Pasteur that serious trouble could arise from the transfer of micro-organisms. Suppose you put a little sour wine into wine that was not sour. The yeast that produced acid would grow in the good wine and turn it sour.

Well, then, suppose a worker was placing wine in casks and got a little on his or her hands. If some of the wine had the acid-producing yeast in it, the worker might have that on his or her hands and, without meaning to, transfer it to good wine. All the wine he or she worked with would turn sour.

If the workers washed their hands every time they began work with a new batch of wine, this might not happen.

Semelweiss was right when he thought the doctors were carrying the disease on their hands. The reason they did not see anything was because micro-organisms might have produced the disease and, of course, you cannot see micro-organisms on your hands.

Such thoughts may have been in Pasteur's mind at the time, but, if so, he could do nothing until he had some evidence that micro-organisms were involved in disease.

4. Germs and disease

Just about the time that Pasteur was completing his experiments that disproved the theory of spontaneous generation, a new crisis was facing France.

In the south, French people grew mulberry bushes and let silkworms feed upon their leaves. From the cocoons of those silkworms (which were really a kind of caterpillar) silk threads were drawn.

The silk industry was important to France and now, suddenly, it was being destroyed. The silkworms were falling sick and were dying, and it seemed that nothing could be done about it.

The call went out for Pasteur—no one but Pasteur. He had saved the wine industry; surely he could save the silk industry. Pasteur protested that he knew nothing about silkworms, but they begged him to come anyway.

In 1865, Pasteur travelled south. Once again he used his microscope. He found micro-organisms present on some of the mulberry leaves but not on others. The silkworms that fed on the infected leaves grew sick and,

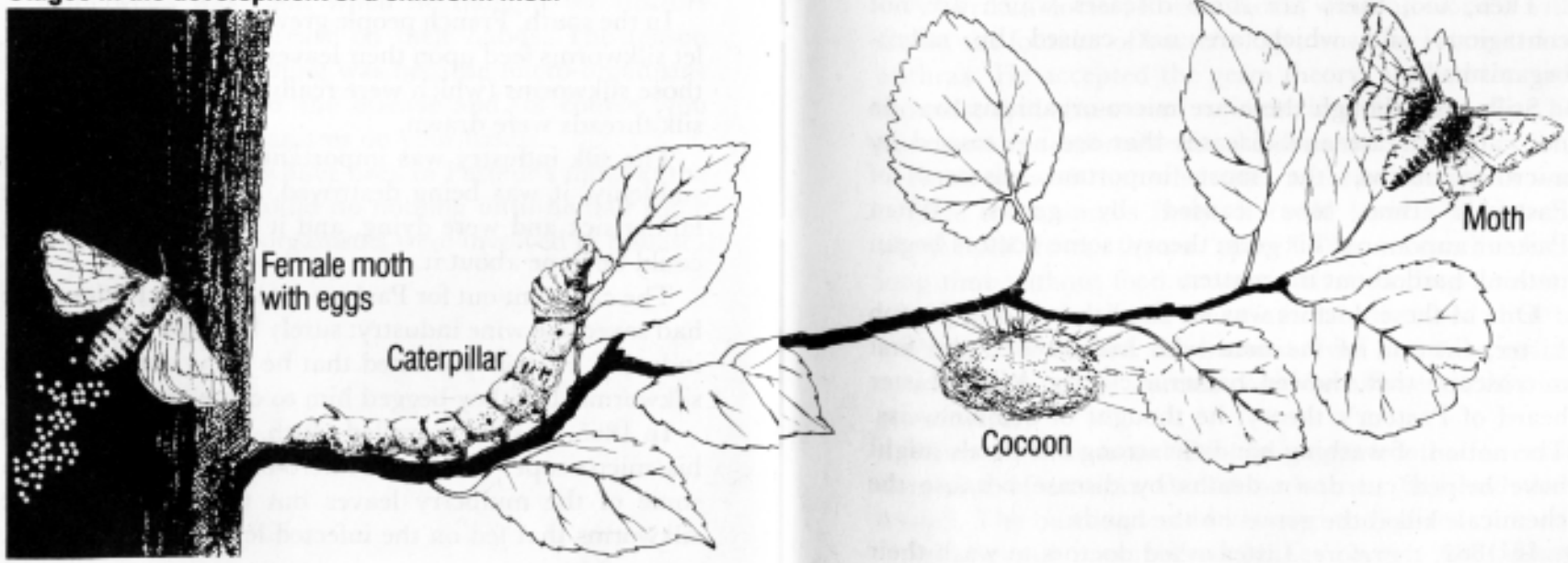
sure enough, those micro-organisms were present in their bodies.

It was clear to Pasteur that these micro-organisms were living and growing inside the silkworms. A small organism that lives and grows in a larger one is called a "parasite". The micro-organism was parasitic on the silkworm.

What was to be done? Wine can be heated to kill yeast. That does not hurt the wine. If silkworms are heated so that the micro-organisms are killed, the silkworms will die also.

Well, then, they had to die. There was no help. The only way to keep the disease from spreading was to destroy all the infected silkworms and all the infected mulberry leaves. A new beginning had to be made with

Stages in the development of a silkworm moth



healthy silkworms and healthy plants.

The people in charge followed Pasteur's advice. It worked. The silk industry was saved.

To Pasteur, it now seemed certain that disease could be caused by a micro-organism. If a disease was "contagious"—that is, if it could be spread from one living thing to another—then it *must* be caused by a micro-organism. Some small parasite is transferred from a sick organism to a healthy one, and then the healthy one gets sick, too.

The micro-organisms can be spread through the air by coughing and sneezing. They can be spread by the hands and other parts of the body. They can be left behind in body wastes. They are too small to see and a healthy person may not know he or she has picked up the

micro-organisms until they start getting sick themselves.

Pasteur announced all this, and it is called "the germ theory of disease".

Many of the micro-organisms that produce disease are bacteria, which are what we usually think of when we speak of germs. However, bacteria are not the only ones responsible. Some diseases are caused by yeasts, protozoa, or other kinds of micro-organisms.

Just because some micro-organisms cause disease, however, does not mean that all of them do. Actually, only a small minority of the different kinds of micro-organisms make trouble for other living creatures. The vast majority live in the soil or in water or in air and are harmless. Many of them are very useful. Some bacteria, for instance, keep the soil fertile. Others decay dead plants and animals and change them into chemicals which other plants and animals can use to grow.

Then, too, there are some diseases which are not contagious and which are not caused by micro-organisms.

Still, even though there are micro-organisms that do not cause disease and diseases that are not caused by micro-organisms, the most important diseases of Pasteur's time *were* caused by germs. When Pasteur announced his germ theory, some doctors began to think hard about the matter.

One of these doctors was an English surgeon, Joseph Lister, the son of the man who had devised the first microscope that showed bacteria clearly. When Lister heard of Pasteur's theory, he thought of Semmelweiss. The notion of washing hands in strong chemicals might have helped cut down deaths by disease because the chemicals killed the germs on the hands.

In 1867, therefore, Lister asked doctors to wash their

hands and their instruments in strong chemicals before they operated. Before that, patients often died of fevers after an operation had been carried through successfully. After the doctors started washing their hands and their instruments, however, the patients stopped dying.

Then, in 1870, France got involved in a war. Pasteur, who was very patriotic, tried to join the army but the French officials told him he was too old since he was almost 50. Besides, he was more important in the laboratory, so Pasteur went to work in the hospitals where he forced the doctors to boil their instruments and steam their bandages before they touched the wounded soldiers. He saved many lives in that way.

After the war, Pasteur became interested in a disease called "anthrax" that affected cattle and sheep. It was very deadly. The very ground in which the dead animals were buried seemed to be full of the disease.

A German doctor, Robert Koch, who had worked with Cohn, the founder of bacteriology, was also interested in anthrax. He accepted the germ theory, studied the sick animals, and discovered a bacterium in them that he thought was responsible for the disease.

Koch showed that when this anthrax bacterium was outside the animal's body, it could form a thick wall about itself. It was then a "spore". A spore can live for a long time without food or water. Even boiling does not kill it. For that reason, when animals that had died of anthrax were buried, the bacteria lived on in the soil as spores and healthy animals could be affected if they ate grass there.

When Pasteur heard this, he suggested that animals that died of anthrax should be burned first and then buried. The burning would kill even the spores.

But Pasteur remembered Jenner's work, too. If any

animal happened to survive anthrax, it never caught the disease again. If there was some mild disease similar to anthrax, the animal could be given the mild disease and would then be immune to anthrax. Unfortunately, there was no mild disease of this sort.

But now that the germ theory was understood, could a bacterium causing a mild disease be developed in the laboratory? Pasteur thought this might be done.

First he collected some of the bacteria from animals sick with anthrax and let them grow in special food. He then took some of the bacteria and heated them. He did not heat them enough to kill them, only enough to half-kill them. They were still alive, but they could barely grow any more.

Suppose he inoculated an animal with these "attenuated" (meaning thinned out and weakened) anthrax bacteria. The animal would not catch a bad case of the disease because the attenuated bacteria would grow so slowly. Still, the animal body, fighting off the attenuated bacteria, might develop a defence that would also work against the normally strong bacteria. Pasteur tried it out and the scheme seemed to work.

In 1881, therefore, he arranged for a public test. He began with a herd of sheep and inoculated half of them with attenuated anthrax bacteria. He then waited for a period of time to let those sheep develop their defences. Once that was done, he inoculated the entire herd with deadly, full-strength anthrax bacteria.

Within a few days every sheep that had *not* previously received the attenuated form became sick and died. Those sheep that *had* received the attenuated form remained healthy. Nobody could argue about the germ theory after that, especially since it showed that doctors might now learn to control diseases.

Anthrax bacteria

Next to Pasteur himself, Robert Koch was the most important of those who were now studying germs in connection with disease. He tried to study the bacteria he obtained from people or animals that were sick with one disease or another.

One problem was that he usually found a large number of different kinds of bacteria. It was hard to tell which ones were responsible for the disease. Instead of using soup in which to grow the germs, he began to use a kind of gelatin called "agar-agar".

He placed the sterile agar-agar at the bottom of a flat dish, and when it cooled it became solid. Then he spread a small bit of bacteria-containing soup over it. There would be one bacterium in one place, another in another place, and so on. Each one would live and multiply in the agar-agar, but none of them would be able to move in the solid material. The different bacteria and their descendants stayed separate and in place. Each original bacterium would soon be surrounded by a mass of its own descendants, and there would be a *colony* consisting of a single kind of bacterium, and no more.

Koch could test each colony separately and then find a particular bacterium that would cause a particular disease. He discovered the bacterium that caused tuberculosis and the one that caused cholera. He even discovered the bacterium that was responsible for the Black Death.

Once the germ was known, it could be used to develop methods for preventing disease. Pasteur's method of heating the bacterium and attenuating it was one way. A German doctor, Emil Adolf von Behring, who had been one of Koch's assistants, discovered another.

Behring found that the defence developed by an animal against a disease was concentrated in its blood. A

Bacteria and moulds growing on agar

bacterium liberated some poison in the blood which caused a disease. This poison was called a "toxin". What was in the blood to defend the organism against the toxin was an "antitoxin". Suppose an animal was suffering from the disease called tetanus, for instance, caused by the tetanus bacterium. Some of the animal's blood could be withdrawn. The blood could be treated in various ways to extract the antitoxin. If the antitoxin was then injected into the blood of a healthy animal, that healthy animal would gain the defences against tetanus that the sick animal had developed. The healthy animal would not get tetanus even if the tetanus bacterium was injected into it. The healthy animal was temporarily immune.

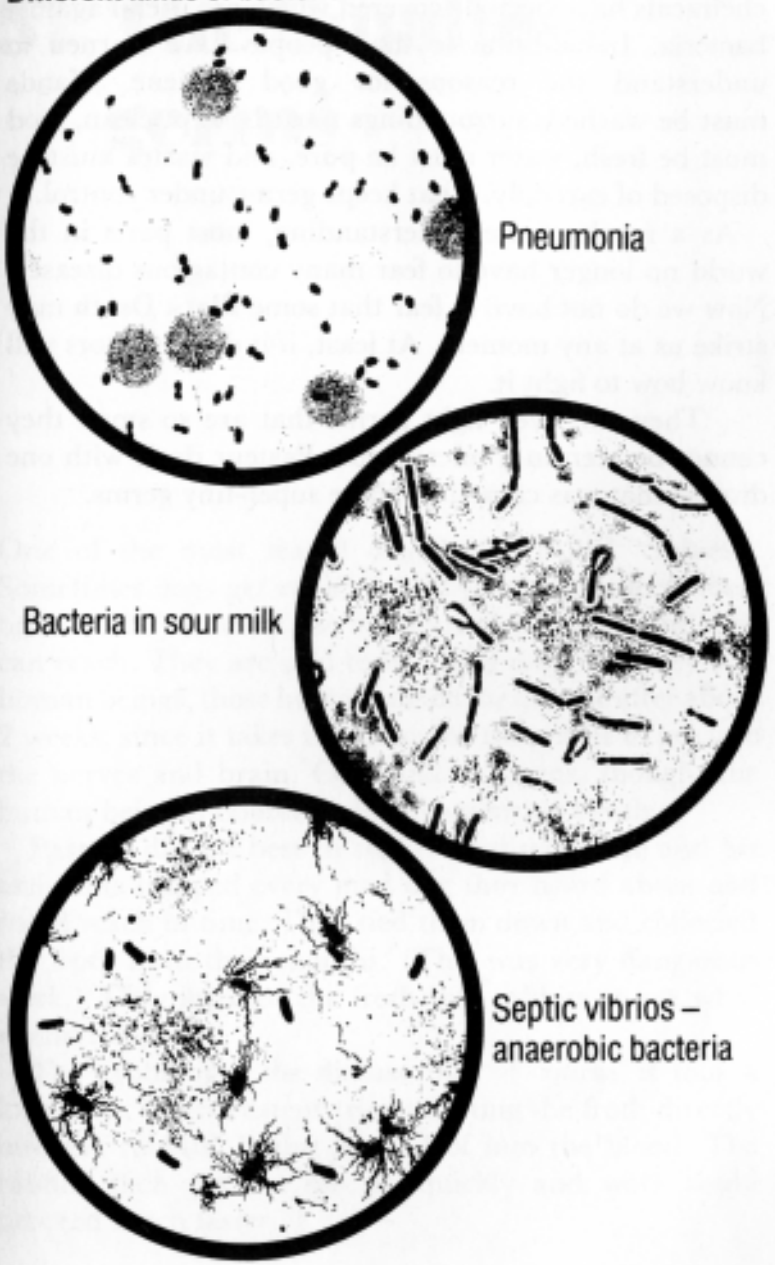
Behring wondered if antitoxins could be developed for other diseases. At the time, one serious disease from which many children suffered was diphtheria. Behring and a friend, another German doctor, Paul Ehrlich, injected the diphtheria bacterium into animals and then took out samples of blood which contained a diphtheria antitoxin.

In 1892, they had a large supply of the diphtheria antitoxin. They found that, not only did it keep healthy children from catching diphtheria, but those who had already caught it were helped to get better. People found they no longer had to fear diphtheria.

Ehrlich went on to try to attack bacteria in another way. Perhaps there were chemicals which, if injected into a sick human being, would kill a disease germ without hurting the sick person. That would certainly help cure the disease. In 1909, he and his assistants found a chemical called "arsphenamine" that seemed to kill the bacterium that caused a disease known as syphilis.

Since the days of Pasteur, Koch, Behring, and Ehrlich, more antitoxins have been developed and more

Different kinds of bacteria



chemicals have been discovered which are useful against bacteria. In addition to that, people have learned to understand the reasons for good hygiene. Hands must be washed, surroundings must be kept clean, food must be fresh, water must be pure, and wastes must be disposed of carefully. That keeps germs under control.

As a result of the understanding, most parts in the world no longer have to fear many contagious diseases. Now we do not have to fear that some Black Death may strike us at any moment. At least, if it does, doctors will know how to fight it.

They can even fight germs that are so small they cannot be seen in a microscope. Pasteur dealt with one disease that was caused by these super-tiny germs.

5. The Smallest germs

One of the most feared diseases is called "rabies". Sometimes dogs get rabies and the sickness affects their brains. They froth at the mouth and bite everyone they can reach. They are said to be "mad dogs". If they bite human beings, those humans catch the disease after about 2 weeks, since it takes that long for the germs to get into the nerves and brain. Once that happens, though, the human being is bound to die an agonising death.

Pasteur did his best to study the disease. He and his assistants trapped every mad dog they heard about and could reach in time. They tied them down and collected the froth from their mouths. (This was very dangerous work.) They injected the froth into rabbits to see what would happen.

The rabbits got the disease but, of course, it took a long time. Then Pasteur tried injecting the froth directly into the rabbits' brains instead of into the blood. The rabbits then got the disease quickly and work could proceed much faster.

Once enough sick rabbits were collected, what could be done? Could Pasteur attenuate the germ as he did the anthrax bacterium? He tried. The germs in the sick rabbits were in the brain and spinal cord. He cut out the spinal cord and heated it gently. Every day he cut off a piece and continued heating the rest.

In this way, he ended with a series of pieces that had been heated for various lengths of time. He soaked each piece in fluid and then injected the fluid into the brains of the healthy rabbits. He found that the longer he had heated the piece the milder the disease it caused. A piece that had been heated for 2 weeks would not give the disease at all.

But would it make an animal immune? Pasteur injected some of his attenuated rabies germ into a healthy dog. Nothing happened. Then he put the dog in a cage with another dog that had rabies. The sick dog promptly began to fight and the healthy dog was bitten. After a while it was rescued and the bites healed. The dog did *not* get rabies.

How could one try it on a human being? You can not deliberately take the chance of giving a human being rabies. But then, on 4 July 1885, a 9–year-old boy named Joseph Meister was badly bitten by a mad dog, and he was rushed to Pasteur as quickly as possible.

Pasteur knew that once the disease reached the nerves and brain young Joseph would die. Joseph had nothing to lose if Pasteur experimented, and it had to be done quickly. Pasteur injected some of his most weakened germs to begin helping the body build defences. He waited a day and injected some less weakened germs. Each day he gave Meister stronger germs as his body's defences developed, until after 11 days Joseph was getting the germs at full strength. He never got rabies!

It was another triumph for Louis Pasteur, and yet there was one catch. In all work with rabies, Pasteur could never find a bacterium, or a germ of any kind, that seemed to cause the disease.

Could it be that the germ theory of disease was wrong? No, Pasteur did not believe that for a moment. Rabies was catching. It could be transferred from one organism to another. *Something* had to be doing the transferring. If nothing could be seen, then maybe it was because the germ was too small to be seen under a microscope.

This seemed to be true for other diseases, also. No one could find the germ for smallpox, for instance, or the germ for chickenpox, or the germ for influenza, or the germ for the common cold. They were all too small to see.

This was also true for certain diseases that affected organisms other than human beings. Tobacco plants, for instance, suffered from a disease that made their leaves wither. When infected, the leaves would look mottled, as though a mosaic pattern had been drawn on them. The disease was therefore called "tobacco mosaic disease".

A Russian scientist, Dmitri Ivanovski, looked for the germ and could not find it. The juice of mashed leaves from sick plants would cause healthy plants to get the disease, but there was no germ in the juice that he could see.

It occurred to Ivanovski to try to filter the juice. If he could force the juice through something that had tiny holes in it—holes too small to be seen in a microscope—it might stop the very small germs. The liquid would pass through the holes without the germs and would not cause the disease.

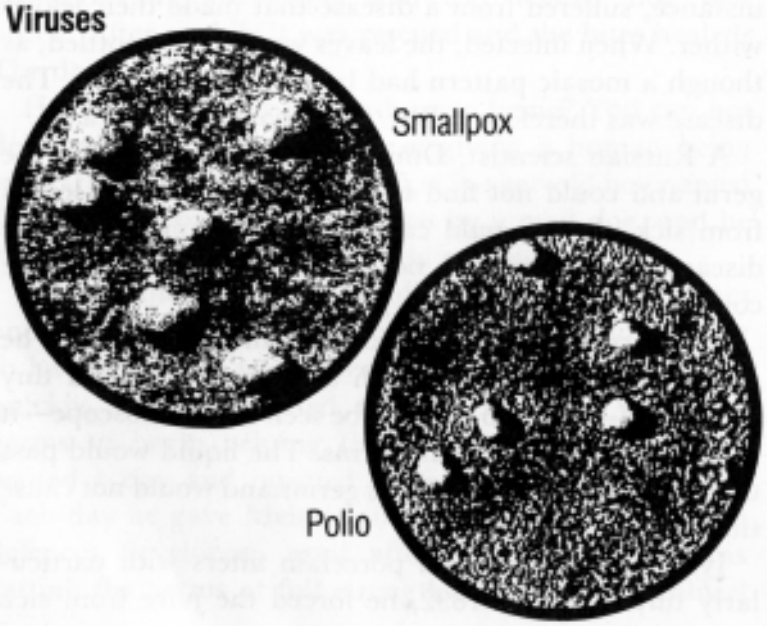
Ivanovski used special porcelain filters with particularly tiny holes. In 1892, he forced the juice from sick

tobacco leaves through the filters. Even the smallest germ would surely be stopped by it.

But it was not. The fluid that came through would still cause tobacco mosaic disease if placed on the leaves of a healthy plant. Ivanovski had to face the fact that the germs, whatever they were, were small enough to go through even the tiny holes in the porcelain filter. He could not believe that any germs could be *that* small and he just stopped experimenting in that direction.

In 1898, a Dutch botanist, Martinus Willem Beijerinck, also tried the same experiment. He, too, passed the juice of mashed tobacco leaves that had the disease through a porcelain filter. He, too, found that the juice that came through could still infect healthy plants.

He was ready, however, to accept the fact that the germs that caused tobacco mosaic disease were small

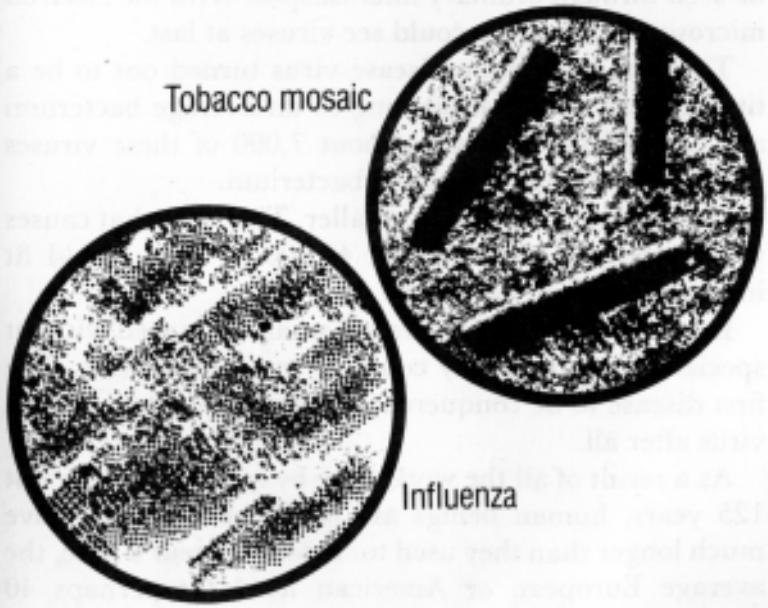


enough to go through the filter. In fact, he thought the germs might be hardly any bigger than the smallest bits (called "molecules") of water, so that they would go through anything water molecules might go through.

A Latin word for a poisonous juice from plants is "virus". It seemed to Beijerinck that the juice from diseased tobacco leaves was poisonous to healthy tobacco plants, so he called it a virus. The name came to be used for the very tiny germs in the juice.

But how tiny were those viruses? Were they really no larger than water molecules? For a long time, no one could tell. Then, in 1931, a British scientist, William Joseph Elford, took up the problem. Why not, he thought, make use of holes still smaller than those in the porcelain filters?

He used collodion instead. Collodion was a thin



transparent membrane, something like cellophane, and it had tiny holes in it. These holes could be made of different sizes, depending on the exact way in which the collodion was prepared. The holes could be made tinier and tinier and tinier.

Elford forced virus juice through collodion that had holes only about a hundredth as wide as the average bacterium. When that collodion was used, the water was forced through but the virus stayed behind. What came through could not cause disease.

That meant that virus particles might be far smaller than bacteria but were still far larger than water molecules.

Later in the 1930s, special microscopes were invented that made use of beams of tiny particles called "electrons" instead of light. These "electron microscopes" could show things far smaller than anything that could be seen through ordinary microscopes. With the electron microscope, scientists could see viruses at last.

The tobacco mosaic disease virus turned out to be a tiny rod less than half as long as an average bacterium and very skinny, indeed. About 7,000 of these viruses could be fitted inside a single bacterium.

Other viruses were even smaller. The virus that causes yellow fever is so small that 40,000 of them would fit inside an average bacterium.

Even though viruses were too small to be seen without special equipment, they could be guarded against. The first disease to be conquered, smallpox, was caused by a virus after all.

As a result of all the work done by scientists in the last 125 years, human beings are much healthier and live much longer than they used to. Before Pasteur's time, the average European or American lived for perhaps 40

years. Nowadays, the average lifetime is about 70 years.

Every one of us has, on the average, some 30 extra years of life because of the work of Pasteur and those who followed him.